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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/498,704	02/07/2000	Paul S. Uster	5325-0162.30	9201

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Alza Corporation
1900 Charleston Road
PO Box 7210, M10-3
Mountain View, CA 94039-7210

EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/498,704	USTER ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2-12-04* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment dated 2-12-04 is acknowledged.

Claims included in the prosecution are 1-30.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant amends Tables 1 and 3 and also the claims and argues that the changes made are not new matter. Applicant does not however, indicate whether original numbers were typographical and why there is enormous discrepancy between the original values and the new values. What did the original numbers represent? According to applicant the molar drug/lipid ratio for each composition described in Table 1 and Table is simply the mole fraction of drug divided by the sum of the lipid mole fractions. The examiner recognizes that; however, what is changed in Table 1 is the concentration of phospholipids now expressed as mg/m1 of phosphorus. There is no explanation for making these changes. Therefore, the changes are deemed to be new matter.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marin (5,213,804) in combination with Mori (Cancer Chemther Pharmacol, 1995) of record, or vice versa.

Martin discloses a liposome compositions containing a phospholipid, 1-20 mol. % of an amphipathic lipid derivatized with PEG. The composition is for localizing an imaging or anti-tumor agent for therapeutic and diagnostic purposes (note the abstract, col. 1, line 34 et seq., Examples and claims).

What is lacking in Martin is the use of a radio sensitizer as the active agent

Mori while disclosing liposomes containing dipalmitoyl-5-fluoro-2-deoxyuridine teaches that treatment of lung metastasis bearing mice with this composition resulted in

significant increase in the median survival time of treated mice as compared to control mice (note the abstract and Materials and Methods).

What is lacking in Mori is the inclusion of lipid derivatized PEG.

The use of the radio sensitizer as the anti-tumor agent in the compositions of Martin would have been obvious to one of ordinary skill in the art because of its effectiveness shown by Mori. Alternately to use the lipid derivatized polymer in the liposomal compositions of Mori would have been obvious to one of ordinary skill in the art because of the increase in the blood circulation time of the liposomes as shown by Martin (note col. 14). Although Mori does not teach other halogen derivatives of deoxyuridine, in the absence of showing otherwise, it is deemed obvious to one of ordinary skill in the art to use halogens other than fluorine taught by Mori with a reasonable expectation of obtaining at least similar results.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant submits another reference (Mori) and argues that the composition described by Mori has a molar drug/lipid ratio of 0.03 whereas in instant invention, the drug amounts are higher. Applicant points out to Mori (1993) and argues that according to Mori, incorporation of lipophilic prodrugs at higher concentrations inhibited the extrusion procedure due to insoluble unincorporated drug molecules. According to applicant, in instant composition, the drug amounts are higher because of the method of preparation used. This argument is not found to be persuasive. First of all, instant claims do not recite a method. Secondly, the primary reference of Martin discloses two methods of preparation of liposomes besides the classical lipid film hydration method

reported by Mori (see columns 11 and 12 of Martin) and applicant has not established that by these methods one cannot obtain higher drug:lipid ratios. Thirdly, Mori's teachings regarding the difficulty in using higher amounts of the active agent pertain to the preparation of smaller sized liposomes using extrusion and therefore, one of ordinary skill in the art would be motivated to use higher amounts of drugs if extrusion and sizing is not required. Instant claims do not recite liposome sizes.

5. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marin (5,213,804) in combination with Mori (Cancer Chemther Pharmacol, 1995) of record, or vice versa as set forth above, further in view of Kassis (5,077,034) of record.

As pointed out above, Mori does not teach iodine derivatives of deoxyuridine as the radiosensitizer. One of ordinary skill in the art would be motivated to use halogens other than fluorine taught by Mori with a reasonable expectation of obtaining at least similar results since Kassis teaches that the halogen derivatives of deoxyuridine, iodo-deoxyuridine derivative in particular is effective in the treatment and diagnosis of tumors (note the abstract, Examples and claims).

Applicants' arguments have been fully considered, but are not found to be persuasive. Applicants' arguments with regard to Martin and Mori have been addressed above. Applicant provides no additional arguments with regard to Kassis. The rejection is maintained.

Claims 10-30 are allowable if applicant overcomes the new matter rejection.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.

Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK